SPECIAL ARTICLES

THE PREDICTION OF THE PHYSIOLOGICAL ACTION OF ALCOHOLS[1]

COMPARATIVELY few laws are known connecting the chemistry of various substances with their physiological effects; such a condition is natural because of the complexity of many of the compounds used in therapeutics. In seeking for generalizations it is therefore advisable to direct our attention at first to compounds possessing rather simple structures.

In connection with the testing of the toxicity of various normal primary alcohols upon *Paramecia* the writer noticed the almost quantitative application of a simple numerical rule. Methyl alcohol, as was expected from its structure, exhibited an abnormaiity, but beginning with ethyl alcohol and expressing its action as *unity* the acute toxicities of the successive members subjected themselves to numerical expression, particularly when the quantity of alcohol used was expressed in moles and not in grams.

In an homologous series of this kind the molar toxicity of any given member is three times that of the preceding member. The rule is expressed numerically by the geometrical progression:

$$1 : 3 : 3^2 : 3^3 : 3^4 : 3^5 \ldots .$$

The value of this generalization, originally presented by Traube on the basis of surface tension experiments, lies in the fact that it may be appplied not merely to unicellular organisms, but to mammals as well. Its application is shown best by a few examples.

EXAMPLE I

The toxic concentration of ethyl alcohol for a given strain of paramecia was found by experiment to be 4.5 per cent. What concentration of *n*-octyl alcohol will prove equally toxic to the same strain of organisms?

Solution: $1 \times 3 \times 3 \times 3 \times 3 \times 3 \times 3 = 729.$

$$\frac{4.5\% \times 2.8^{*}}{729} = 0.02\% = \text{calculated concentration.}$$ [2]

The observed value was found to be 0.03 per cent.

[1] Article No. 4, Chemical Research Department, Parke, Davis & Co.

EXAMPLE II

If a mouse is killed within a few hours by intraperitoneal administration of 12 mg. of ethyl alcohol per gram of body weight, what will be the corresponding toxic dose of *n*-amyl alcohol?

Solution: $1 \times 3 \times 3 \times 3 = 27.$

$$\frac{12 \text{ mg.} \times 1.9^{*}}{27} = 0.84 \text{ mg.}$$

The observed value was found to be very close to 1.0 mg. per gram of body weight.

EXAMPLE III

The toxic dose of ethyl alcohol when injected into the blood stream of the cat was found by Macht[3] to be 5.0 c.c. per kilo. The administration time was 50 minutes. Under exactly similar experimental conditions what will be the toxic dose (*a*) of *n*-propyl alcohol, (*b*) of *n*-amyl alcohol?

Solution: (*a*) $1 \times 3 = 3.$

$$\frac{5.0 \text{ c.c.} \times 1.3^{*}}{3} = 2.17 \text{ c.c.}$$

$$= 2.14 \text{ c.c. corrected for sp. gr.}$$

The experimental value was found by Macht to be 2.0 c.c., although in this case the toxic amount of liquid was administered during 20 minutes.

Solution: (*b*) $1 \times 3 \times 3 \times 3 = 27.$

$$\frac{5.0 \times 1.9^{*}}{27} = 0.35 \text{ c.c. (uncorrected for sp. gr.).}$$

The experimental value was found to be 0.15 c.c., which is a very satisfactory result in view of the fact that the toxic material was administered during seven minutes. When administered over an interval of from 30 to 50 minutes the observed value would no doubt approach the calculated value.

A more detailed discussion of the present work is appearing in a series of reports in the *J. Am. Pharm. Association.*

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[2] The values marked with the asterisk are molecular weight ratios which serve to convert the predicted values from moles to grams.

[3] *J. Pharmacol.*, 16, 1 (1920).